TITLE: Antidepressant Use for Pregnant and Nursing Women: Comparative Safety and Optimal Use

DATE: 02 March 2011

RESEARCH QUESTIONS

1. What is the comparative safety of antidepressant agents in pregnant and nursing women?

2. What are the evidence-based guidelines for the use of antidepressant agents in pregnant and nursing women?

KEY MESSAGE

The conclusions presented in the literature indicate that paroxetine should be avoided during pregnancy due to an increased risk of cardiovascular malformation; however, no other major contraindications to antidepressant use during pregnancy or breastfeeding were identified.

METHODS

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 2, 2011) University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between January 1, 2006 and February 14, 2011. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, and guidelines. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.
RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed evidence-based guidelines.

Five systematic reviews and meta-analyses and three evidence-based guidelines were identified regarding the use of antidepressant agents in pregnant and nursing women. No relevant health technology assessments were identified. Additional articles of potential interest, including a number of review articles, can be found in the appendix.

OVERALL SUMMARY OF FINDINGS

Authors of all included SRs examining the effects of antidepressants during pregnancy concluded that paroxetine exposure during the first trimester carries a risk of cardiovascular malformation.\(^1\)-\(^3\) Conflicting results were identified regarding selective serotonin reuptake inhibitor (SSRI) exposure and the risk of persistent pulmonary hypotension in the nonate\(^2\) and infants of women taking SSRIs were found to undergo twice as many electrocardiograms in their first year when compared to infants not exposed.\(^3\) No significant differences were observed between children exposed, or not exposed, to antidepressants in studies investigating developmental outcomes.\(^2\)

The clinical guidelines\(^6\)-\(^8\) made the following statements regarding antidepressant use during pregnancy:

- No single antidepressant has been deemed more effective than any other.\(^6\)
- Choice of antidepressant treatment should be based on the women’s symptoms, family history, past treatment, and previous experience with antidepressants.\(^6\)
- Treatment with a single drug at a higher dose is favoured over treatment with multiple drugs at lower doses.\(^7\)
- SSRI exposure after 20 weeks gestation may be associated with an increased risk of persistent pulmonary hypertension in the neonate.\(^8\)
- Tricyclic antidepressants (TCAs) have the lowest known risk profile of the antidepressants during pregnancy and breastfeeding.\(^8\)
- With the exception of paroxetine, SSRIs show no reported risks greater than any other class of antidepressants.\(^8\)
- Fluoxetine is the lowest risk SSRI.\(^8\)
- Paroxetine should be avoided during pregnancy\(^7\),\(^8\) or when planning to become pregnant\(^7\) as it is associated with possible cardiovascular defects.

The included SRs concluded that there is not a clear contraindication for most antidepressants while breastfeeding\(^4\) but that the tolerability of these drugs by both mothers and babies is not well described in the literature.\(^5\) Nortriptyline and SSRIs have shown favorable safety to mother and child while breastfeeding.\(^5\) The authors suggested the use of doxepine and nefazodone be avoided and that fluoxetine be used carefully.\(^4\)

The clinical guidelines\(^7\)-\(^8\) made the following statements regarding antidepressant use while breastfeeding:
If the woman has successfully been treated with SSRIs, TCAs, or serotonin-norepinephrine reuptake inhibitors (SNRIs) in the past, the safety data for that drug should be reviewed and be continued as first-line treatment if there are no contraindications.\textsuperscript{7}

- Relatively low levels of TCAs are detected in breast milk.\textsuperscript{8}
- Relatively high levels of fluoxetine and citalopram are detected in breast milk.\textsuperscript{8}
REFERENCES SUMMARIZED

Health technology assessments
No literature identified.

Systematic reviews and meta-analyses

**Pregnancy**


**Breastfeeding**


Guidelines and recommendations


See: Management of depression, page 10 and Chapter 7: Pharmacological Treatment of Mental disorders in Pregnant and Breastfeeding Women
APPENDIX – FURTHER INFORMATION:

Systematic reviews and meta-analyses – non-comparative


Clinical practice guidelines and recommendations – methodology not stated


This statement was reaffirmed by the Canadian Paediatric Society (CPS) 2009 Jan. http://www.cps.ca/english/statements/PP/pp04-03.htm#Treatment


Review articles

Pregnancy


**Breastfeeding**


**Additional references**


